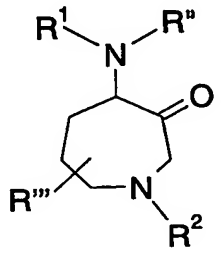
What is claimed is:

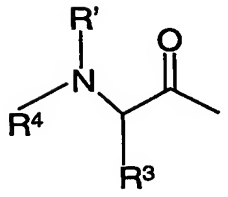
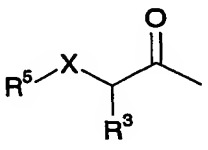
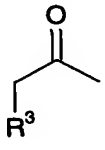
1. A method for treating a disease by inhibiting cathepsin S comprising administering at least one compound of Formula I neat or in a pharmaceutically acceptable formulation in an effective amount to a mammal in need thereof, wherein Formula I comprises:



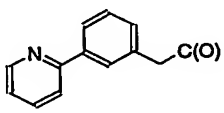
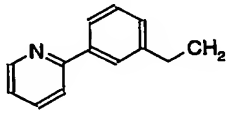
I

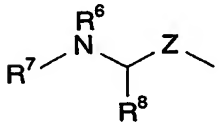
wherein:

$R^1$ is

 (a);  (b) or  (c);

$R^2$ is H, $C_{1-6}$alkyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl, Het-$C_{0-6}$alkyl, $R^9C(O)$-, $R^9C(S)$-, $R^9SO_2$-, $R^9OC(O)$-,

$R^9R^{11}NC(O)$-, $R^9R^{11}NC(S)$-, $R^9(R^{11})NSO_2$-  ,  of

 ;

$R^3$ is H or substituted or unsubstituted $C_{1-6}$alkyl, $C_{3-7}$cycloalkyl$C_{0-6}$alkyl, $C_{4-7}$cycloalkenyl$C_{0-6}$alkyl, $C_{5-8}$bicycloalkyl$C_{0-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, Het$C_{0-6}$alkyl, Ar$C_{0-6}$alkyl, Ar-Ar$C_{0-6}$alkyl, Ar-Het$C_{0-6}$alkyl, Het-Ar$C_{0-6}$alkyl, or Het-Het$C_{0-6}$alkyl;

$R^4$ is H, $C_{1-6}$alkyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl, Het-$C_{0-6}$alkyl, $R^5C(O)$-, $R^5C(S)$-, $R^5SO_2$-, $R^5NSO_2$-, $R^5OC(O)$-, $R^5R^{12}NC(O)$-, or $R^5R^{12}NC(S)$-;

$R^5$ is H, $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl, Ar-Ar$C_{0-6}$alkyl, Ar-Het$C_{0-6}$alkyl, Het-Ar$C_{0-6}$alkyl, Het-Het$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

$R^6$ is H, $C_{1-6}$alkyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

$R^7$ is H, $C_{1-6}$alkyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl, Het-$C_{0-6}$alkyl, $R^{10}C(O)$-, $R^{10}C(S)$-, $R^{10}SO_2$-, $R^{10}OC(O)$-, $R^{10}R^{13}NC(O)$-, or $R^{10}R^{13}NC(S)$-;

$R^8$ is H, $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, Het$C_{0-6}$alkyl or Ar$C_{0-6}$alkyl;

$R^9$ is $C_{1-6}$alkyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl or Het-$C_{0-6}$alkyl;

$R^{10}$ is $C_{1-6}$alkyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl or Het-$C_{0-6}$alkyl;

$R^{11}$ is H, $C_{1-6}$alkyl, Ar-$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

$R^{12}$ is H, $C_{1-6}$alkyl, Ar-$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

$R^{13}$ is H, $C_{1-6}$alkyl, Ar-$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

R'is H, $C_{1-6}$alkyl, Ar-$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

R"is H, $C_{1-6}$alkyl, Ar-$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

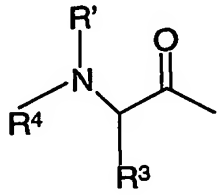
R'" is $C_{1-6}$alkyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

X is $CH_2$, S, or O;

Z is C(O) or $CH_2$; or

a pharmaceutically acceptable salt, hydrate or solvate thereof.

2. The method of claim 1 wherein, in Formula:




$R^1$ is (a);

$R^2$ is $R^9SO_2$ $R^9OC(O)$-, or $R^9C(O)$-;

$R^3$ is $C_{5-7}$cycloalkyl$C_{1-2}$alkyl, $C_{4-5}$cycloalkenyl$C_{1-2}$alkyl, $C_{5-8}$bicycloalkyl$C_{1-2}$alkyl or Ar-Het$C_{0-6}$alkyl;

$R^4$ is $R^5C(O)$-, or $R^5SO_2$-;

$R^5$ is unsubstituted or substituted furanyl, tetrahydrofuranyl, morpholinyl, pyrrolyl, piperazinyl, pyrazolyl, isoxazolyl, thiazolyl, pyrazolyl, pyrazolo[5,1-c]pyrimidinyl, triazolyl, pyrazinyl, imadazolyl, benzofuranyl, thiophenyl, furo[3,2-b]-pyridine-2-yl, phenyl, pyridinyl, thieno[3,2-b]thiopheneyl, or unsubsituted or $C_{1-2}$alkylsubstituted pyrazolo[5,1-c]triazinyl;

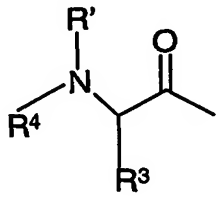
$R^9$ is Het$C_{0-6}$alkyl, Ar$C_{0-6}$alkyl, or $C_{1-6}$alkyl;

R'is H, $C_{1-6}$alkyl;

R"is H or $C_{1-6}$alkyl; and

R"' is $C_{1-6}$alkyl.

3. The method of claim 1 or 2 wherein in Formula I,



$R^1$ is (a)

$R^2$ is $R^9SO_2$ $R^9OC(O)$-, or $R^9C(O)$-;

$R^3$ is cyclopentylmethyl, cyclopentylethyl, cyclopentenylmethyl, cyclopentenylethyl, cyclohexylmethyl, 4-methylcyclohexylmethyl, 2-cyclohexylprop-1-yl, cyclohexylethyl, cycloheptylmethyl, 7,7-dimethylbicyclo[2.2.1]hept-1ylmethyl, or indol-2-ylmethyl;

$R^4$ is $R^5C(O)$- or $R^5SO_2$-

$R^5$ is furan-2-yl, furan-3-yl, 2-methylfuran-3-yl, 2,4-dimethylfuran-3-yl, 5-phenylfuran-2-yl, 5-(2-chlorophenyl)furan-2-yl, 5-(3-chlorophenyl)furan-2-yl, 5-(4-chlorophenyl)furan-2-yl, 5-(4-fluorophenyl)furan-2-yl, 5-(4-hydroxyphenyl)furan-2-yl, 5-(3-trifluoromethylphenyl)furan-2-yl, 5-(4-trifluoromethylphenyl)furan-2-yl, 5-(3-trifluoromethylphenyl)furan-2-yl, 5-(4-methylphenyl)furan-2-yl, 5-(4-acetylphenyl)furan-2-yl, or 5-trifluoromethylfuran-2-yl;

tetrahydrofuran-2-yl or tetrahydrofuran-3-yl

N-morpholinyl;

pyrrol-2-yl;

piperzin-1-yl or 4-methylpeperzin-1-yl;

1H-pyrazol-2-yl, 1H-pyrazol-4-yl, 1-methyl-2H-pyrazol-2-yl, 2-methyl-2H-pyrazol-2-yl, 1-methyl-2H-pyrazol-3-yl or 2-methyl-2H-pyrazol-3-yl;

isoxazol-5-yl, 3-methylisoxazol-4-yl, 5-methylisoxazol-3-yl, 5-methylisoxazol-4-yl, or 3,5-dimethylisoxazol-4-yl;

thiazol-2-yl, 2-methylthiazol-2-yl, 2,4-dimethylthiazol-5-yl, 2-(2,3-dihydrobenzo[1,4]dioxin-2-yl)thiazol-4-yl, or 4-methyl-2-phenylthiazol-5-yl;

4,7-dimethylpyrazolo[5,1-c]triazin-3-yl;

2-methyl-2H-pyrazol-2-yl;

2,7-dimethylpyrazol[5,1-c]pyrimidin-6-yl;

3-phenyl-3H-{1,2,3]triazol-3-yl;

pyrazin-2-yl or 5-methylpyrazin-2-yl;

1-H-imidazol-2-yl, 1-methyl-1H-imidazol-4-yl or 1-methyl-1H-imidazol-2-yl;

benzofuran-2-yl, 5,6-dimethoxybenzofuran-2-yl, or 5-(2-morpholin-4-yl-ethoxy)benzofuran-2-yl;

thiophene-3-yl, or thiophen-2-yl, 5-pyridin-2-ylthiophen-2-yl, 5-methylthiophenyl 3-methylthiophen-2-yl; or 3-ethoxythiophen-2-yl;

furo[3,2-b]-pyridine-2-yl or 3-methylfuro[3,2-b]pyridin-2-yl;

phenyl, 4-methylphenyl, 3-chlorophenyl, 4-chlorophenyl, 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 2-chlorophenyl, 4-fluorophenyl, 4-hydroxyphenyl, or 4-acetylphenyl;

pyridin-2-yl; or

thieno[3,2-b]thiophen-2-yl or 5-isoxazol-3-ylthiophen-2-yl;

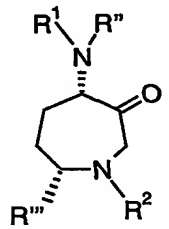
$R^9$ is pyridin-2-yl, 1-oxypyridin-2-yl, phenyl, furan-2-yl or methyl;

R' is H;

R" is H or $C_{1-6}$alkyl; and

R"' is methyl.

4. The method according to any one of claims 1 - 3 wherein Formula I has the structure:



and groups $R^1$ - $R^{13}$, X, Z, R', R" and R"' are the same as defined in any one of claims 1 - 4.

5. The method according to claim 1 wherein the compound of Formula I is morpholine 4-carboxylic acid {(S)-2-[1-methylcyclopentyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

morpholine 4-carboxylic acid {(L)-2-[1-methylcyclopentyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

morpholine 4-carboxylic acid {(S)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

morpholine 4-carboxylic acid {(L)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

furan-carboxylic acid {(S)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

furan-carboxylic acid {(L)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

furan-carboxylic acid {(S)-2-[4-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

furan-carboxylic acid {(S)-2-[homocyclopentyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

morpholine 4-carboxylic acid {(S)-2-[homocyclopentyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

furan-carboxylic acid {(S)-2-[cycloheptyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

morpholine 4-carboxylic acid {(S)-2-[cycloheptyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

furan-carboxylic acid {(S)-2-[cyclopentenyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

furan-carboxylic acid {(S)-2-[tryptophanyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

morpholine 4-carboxylic acid {(S)-2-(7,7-dimethyl-bicyclo[2.2.1]hepty-1-yl)-1-[(4S,7R)-7-methyl-3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

2-methyl-2H-pyrazole-3-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

1H-pyrazole-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

1-methyl-1H-pyrrole-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

isoxazole-5-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

thiazole-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-trifluoromethyl-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

1H-pyrazole-4-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

tetrahydrofuran-3-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

4,7-dimethyl-pyrazolo[5,1-c][1,2,4]triazine-3-carboxylic acid {(S)-2-cyclopentyl-1-[(4S,7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

2,7-dimethyl-pyrazolo[5,1-a]pyrimidine-6-carboxylic acid {(S)-2-cyclopentyl-1-[(4S,7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

3-phenyl-3H-[1,2,3]triazole-4-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

2-(2,3-dihydro-benzo[1,4]dioxin-2-yl)-thiazole-4-carboxylic acid {(S)-2-cyclopentyl-1-[(4S,7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide

N-{(S)-2-cyclopentyl-1-[(4S,7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-2-pyrazol-1-yl-benzamide;

4-methyl-2-phenyl-thiazole-5-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-(4-chloro-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-(3-trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-(2-chloro-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-(4-fluoro-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-(4-methoxy-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-phenyl-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-(4-trifluoromethyl-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-(3-chloro-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-(4-methylphenyl)furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-(4-acetyl-phenyl)-furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

4-methyl-piperazine-1-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

piperazine-1-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

morpholine 4-carboxylic acid {(S)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-meyhanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

morpholine 4-carboxylic acid {(L)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-methanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

2-methyl-thiazole-4-carboxylic acid {(S)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-meyhanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

2-methyl-thiazole-4-carboxylic acid {(L)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-methanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

morpholine 4-carboxylic acid {(S)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-meyhanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

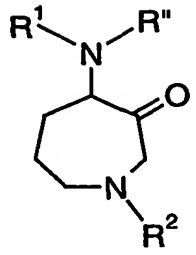
morpholine 4-carboxylic acid {(L)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-methanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

2-methyl-thiazole-4-carboxylic acid {(S)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-meyhanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

2-methyl-thiazole-4-carboxylic acid {(L)-2-[1-methylcyclohexyl-1-(4S,7R)-7-methyl-3-oxo-1-(1-pyridin-2-yl-methanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide; or a pharmaceutically acceptable salt, hydrate or solvate thereof.

6. The method of claim 1 wherein the inhibition of cathepsin S effects treatment or prevention of an autoimmune disease; treatment or prevention of a disease caused by the formation of atherosclerotic lesions and complications arising therefrom; and diseases requiring inhibition, for therapy, of a class II MHC-restricted immune response, inhibition of an asthmatic response, inhibition of an allergic response, inhibition of immune response against a transplanted organ or tissue, or inhibition of elastase activity in atheroma.

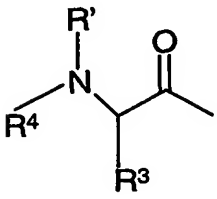
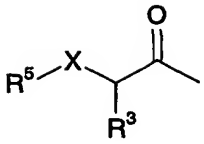
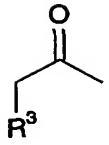
7. A compound of Formula II



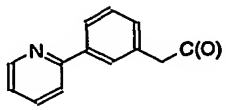
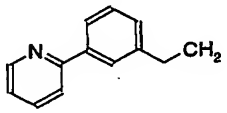
II

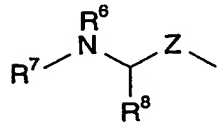
wherein:

$R^1$ is:


;  or  ;

$R^2$ is H, $C_{1-6}$alkyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl, Het-$C_{0-6}$alkyl, $R^9C(O)$-, $R^9C(S)$-, $R^9SO_2$-, $R^9OC(O)$-,

$R^9R^{11}NC(O)$-, $R^9R^{11}NC(S)$-, $R^9(R^{11})NSO_2$-  ,  of


;

$R^3$ is H or substituted or unsubstituted $C_{1-6}$alkyl, $C_{3-7}$cycloalkyl$C_{0-6}$alkyl, $C_{4-7}$cycloalkenyl$C_{0-6}$alkyl, $C_{5-8}$bicycloalkyl$C_{0-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, Het$C_{0-6}$alkyl, Ar$C_{0-6}$alkyl, Ar-Ar$C_{0-6}$alkyl, Ar-Het$C_{0-6}$alkyl, Het-Ar$C_{0-6}$alkyl, or Het-Het$C_{0-6}$alkyl;

$R^4$ is H, $C_{1-6}$alkyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl, Het-$C_{0-6}$alkyl, $R^5C(O)$-, $R^5C(S)$-, $R^5SO_2$-, $R^5NSO_2$-, $R^5OC(O)$-, $R^5R^{12}NC(O)$-, or $R^5R^{12}NC(S)$-;

$R^5$ is H, $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl, Ar-Ar$C_{0-6}$alkyl, Ar-Het$C_{0-6}$alkyl, Het-Ar$C_{0-6}$alkyl, Het-Het$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

$R^6$ is H, $C_{1-6}$alkyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

$R^7$ is H, $C_{1-6}$alkyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl, Het-$C_{0-6}$alkyl, $R^{10}C(O)$-, $R^{10}C(S)$-, $R^{10}SO_2$-, $R^{10}OC(O)$-, $R^{10}R^{13}NC(O)$-, or $R^{10}R^{13}NC(S)$-;

$R^8$ is H, $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, Het$C_{0-6}$alkyl or Ar$C_{0-6}$alkyl;

$R^9$ is $C_{1-6}$alkyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl or Het-$C_{0-6}$alkyl;

$R^{10}$ is $C_{1-6}$alkyl, $C_{3-6}$cycloalkyl-$C_{0-6}$alkyl, Ar-$C_{0-6}$alkyl or Het-$C_{0-6}$alkyl;

$R^{11}$ is H, $C_{1-6}$alkyl, Ar-$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

$R^{12}$ is H, $C_{1-6}$alkyl, Ar-$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

$R^{13}$ is H, $C_{1-6}$alkyl, Ar-$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

R' is H, $C_{1-6}$alkyl, Ar-$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

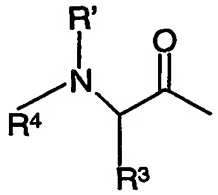
R" is $C_{1-6}$alkyl, Ar-$C_{0-6}$alkyl, or Het-$C_{0-6}$alkyl;

X is $CH_2$, S, or O;

Z is C(O) or $CH_2$; or

a pharmaceutically acceptable salt, hydrate or solvate thereof.

8. A compound of Formula I according to claim 7 wherein:



$R^1$ is (a);

$R^2$ is $R^9SO_2$, $R^9OC(O)$-, $R^9C(O)$- or $C_{1-6}$alkyl;

$R^3$ is $C_{5-7}$cycloalkyl$C_{1-2}$alkyl, $C_{4-5}$cycloalkenyl$C_{1-2}$alkyl, $C_{5-8}$bicycloalkyl$C_{1-2}$alkyl or Ar-Het$C_{0-6}$alkyl;

$R^4$ is $R^5C(O)$-, or $R^5SO_2$-;

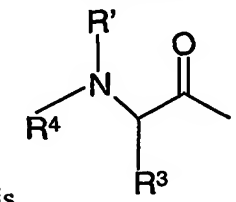
$R^5$ is unsubstituted or substituted furanyl, tetrahydrofuranyl, morpholinyl, pyrrolyl, piperazinyl, pyrazolyl, isoxazolyl, thiazolyl, pyrazolyl, pyrazolo[5,1-c]pyrimidinyl, triazolyl, pyrazinyl, imadazolyl, benzofuranyl, thiophenyl, furo[3,2-b]-pyridine-2-yl, phenyl, pyridinyl, thieno[3,2-b]thiopheneyl, or unsubsituted or $C_{1-2}$alkylsubstituted pyrazolo[5,1-c]triazinyl;

$R^9$ is Het-$C_{0-6}$alkyl, Ar$C_{0-6}$alkyl or $C_{1-6}$alkyl;

R' is H, $C_{1-6}$alkyl; and

R" is H or $C_{1-6}$alkyl.

9 A compound of Formula II according to claim 8 wherein:



$R^1$ is (a)

$R^2$ is $R^9SO_2$ $R^9OC(O)$-, or $R^9C(O)$-;

$R^3$ is cyclopentylmethyl, cyclopentylethyl, cyclopentenylmethyl, cyclopentenylethyl, cyclohexylmethyl, 4-methylcyclohexylmethyl, 2-cyclohexylprop-1-yl, cyclohexylethyl, cycloheptylmethyl, 7,7-dimethylbicyclo[2.2.1]hept-1ylmethyl, or indol-2-ylmethyl;

$R^4$ is $R^5C(O)$- or $R^5SO_2$-

$R^5$ is furan-2-yl, furan-3-yl, 2-methylfuran-3-yl, 2,4-dimethylfuran-3-yl, 5-phenylfuran-2-yl, 5-(2-chlorophenyl)furan-2-yl, 5-(3-chlorophenyl)furan-2-yl, 5-(4-chlorophenyl)furan-2-yl, 5-(4-fluorophenyl)furan-2-yl, 5-(4-hydroxyphenyl)furan-2-yl, 5-(3-trifluoromethylphenyl)furan-2-yl, 5-(4-trifluoromethylphenyl)furan-2-yl, 5-(3-trifluoromethylphenyl)furan-2-yl, 5-(4-methylphenyl)furan-2-yl, 5-(4-acetylphenyl)furan-2-yl, or 5-trifluoromethylfuran-2-yl;

tetrahydrofuran-2-yl or tetrahydrofuran-3-yl

N-morpholinyl;

pyrrol-2-yl;

piperzin-1-yl or 4-methylpeperzin-1-yl;

1H-pyrazol-2-yl, 1H-pyrazol-4-yl, 1-methyl-2H-pyrazol-2-yl, 2-methyl-2H-pyrazol-2-yl, 1-methyl-2H-pyrazol-3-yl or 2-methyl-2H-pyrazol-3-yl;

isoxazol-5-yl, 3-methylisoxazol-4-yl, 5-methylisoxazol-3-yl, 5-methylisoxazol-4-yl, or 3,5-dimethylisoxazol-4-yl;

thiazol-2-yl, 2-methylthiazol-2-yl, 2,4-dimethylthiazol-5-yl, 2-(2,3-dihydrobenzo[1,4]dioxin-2-yl)thiazol-4-yl, or 4-methyl-2-phenylthiazol-5-yl;

4,7-dimethylpyrazolo[5,1-c]triazin-3-yl;

2-methyl-2H-pyrazol-2-yl;

2,7-dimethylpyrazol[5,1-c]pyrimidin-6-yl;

3-phenyl-3H-{1,2,3]triazol-3-yl;

pyrazin-2-yl or 5-methylpyrazin-2-yl;

1-H-imidazol-2-yl, 1-methyl-1H-imidazol-4-yl or 1-methyl-1H-imidazol-2-yl;

benzofuran-2-yl, 5,6-dimethoxybenzofuran-2-yl, or 5-(2-morpholin-4-yl-ethoxy)benzofuran-2-yl;

thiophene-3-yl, or thiophen-2-yl, 5-pyridin-2-ylthiophen-2-yl, 5-methylthiophenyl 3-methylthiophen-2-yl; or 3-ethoxythiophen-2-yl;

furo[3,2-b]-pyridine-2-yl or 3-methylfuro[3,2-b]pyridin-2-yl;

phenyl, 4-methylphenyl, 3-chlorophenyl, 4-chlorophenyl, 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 2-chlorophenyl, 4-fluorophenyl, 4-hydroxyphenyl, or 4-acetylphenyl;

pyridin-2-yl; or

thieno[3,2-b]thiophen-2-yl or 5-isoxazol-3-ylthiophen-2-yl;

$R^9$ is pyridin-2-yl, phenyl, furan-2-yl or methyl;

R' is H; and

R" is H or $C_{1-6}$alkyl.

10. A compound of Formula II according to any one of claims 7 - 9 wherein:

furan-2-carboxylic acid {(S)-2-homocyclohexyl-1-[3-oxo-1-(1-oxy-pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

furan-2-carboxylic acid {(S)-2-tryptophanyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-trifluoromethyl-furan-2-carboxylic acid {(S)-2-cyclohexyl-1-[(s)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

2,4-dimethyl-thiazole-5-carboxylic acid {(S)-2-cyclohexyl-1-[(s)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-methyl-pyrazine-2-carboxylic acid {(S)-2-cyclohexyl-1-[(s)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

1-methyl-1H-imidazole-2-carboxylic acid {(S)-2-cyclohexyl-1-[(s)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

1H-pyrazole-4-carboxylic acid {(S)-2-cyclohexyl-1-[(s)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

4-methyl-2-phenyl-thiazole-5-carboxylic acid {(S)-2-cyclohexyl-1-[(s)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

2,5-dimethyl-furan-3-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

2-methyl-furan-3-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

isoxazole-5-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-methyl-isoxazole-3-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

5-methyl-isoxazole-4-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

3-methyl-isoxazole-4-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

2-methyl-2H-pyrazole-3-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

pyrazine-2-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

thiazole-2-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

2-methyl-thiazole-4-carboxylic acid {(S)-2-cyclohexyl-1-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide;

(S)-3-cyclohexyl-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-2-(thiophene-2-sulfonylamino)-propionamide;

(S)-3-cyclohexyl-2-(1-methyl-1H-imdiazole-4-sulfonylamino)-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-propionamide;

(S)-3-cyclohexyl-2-(3,5-dimethyl-isoxazole-4-sulfonylamino)-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-propionamide;

(S)-3-cyclohexyl-2-(furan-2-sulfonylamino)-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-propionamide;

(S)-3-cyclohexyl-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-2-(pyridine-2-sulfonylamino)-propionamide;

(S)-3-cyclohexyl-2-(morpholine-4-sulfonylamino)-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-propionamide;

(S)-3-cyclohexyl-2-(5-isoxazol-3-yl-thiophene-2-sulfonylamino)-N-[(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl]-propionamide;

4-{(S)-3-cyclopentyl-2-[(1-furan-2-yl-methanoyl)-amino]-propanoylamino}-3-oxo-azepane-1-carboxylic acid benzyl ester;

furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]ethyl}-amide;

furan-2-carboxylic acid [(S)-2-cyclopentyl-1-(1-methanesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-ethyl]-amide;

furan-2-carboxylic acid [(S)-1-(1-benzenesulfonyl-3-oxo-azepan-4-ylcarbamoyl)-2-cyclopentyl-ethyl]-amide

furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[1-(1-furan-2-yl-methanoyl)-3-oxo-azepan-4-ylcarbamoyl]-ethyl}-amide;

furan-2-carboxylic acid {(S)-2-cyclopentyl-1-[3-oxo-1-(1-phenyl-methanoyl)-azepan-4-ylcarbamoyl]-ethyl}-amide; or

piperazine-1-carboxylic acid {(S)-2-cyclopentyl-1-[(4S, 7R)-7-methyl-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl}-amide; or

a pharmaceutically acceptable salt, hydrate or solvate thereof.